

We claim:

1. An isolated antigen or fragment thereof which is immunologically accessible on greater than 50% of known strains of *Neisseria meningitidis*.
2. The isolated antigen or fragment of claim 1 which is immunologically accessible on about 99% of known strains of *Neisseria meningitidis*.
3. The isolated antigen or fragment of claim 1 in which immunological accessibility is determined by using an agglutination assay, an ELISA, a RIA, an immunoblotting assay, a dot-enzyme assay, a surface accessibility assay, or a combination of these assays.
4. The isolated antigen or fragment of claim 1 which is a protein.
5. The protein of claim 4 which has a molecular weight of about 22 kilodaltons.
6. The protein of claim 4 which has a molecular weight of about 18 kilodaltons.
7. The protein of claim 5 which has the amino acid sequence selected from the sequences of: Figure 1 (SEQ ID NO:2), Figure 8 (SEQ ID NO:4), Figure 9 (SEQ ID NO:6), and Figure 10 (SEQ ID NO:8).
8. The protein of claim 5 which has the amino acid sequence of Figure 1 (SEQ ID NO:2).
9. The protein of claim 5 in substantially pure form.

10. The protein of claim 9, wherein said substantially pure form is obtained by the steps of:

- a) isolating a culture of *Neisseria meningitidis* bacteria,
- b) isolating an outer membrane portion from the culture of the bacteria; and
- c) isolating said antigen from the outer membrane portion.

11. The protein of claim 10, wherein step (c) includes the additional step of treating the outer membrane portion with proteinase K followed by protein fractionation.

12. A DNA sequence encoding at least a portion of at least one antigen of the *Neisseria meningitidis* 22 kDa surface protein, said sequence being selected from the group consisting of:

- a) the DNA sequence of Figure 1 (SEQ ID NO:1);
- b) the DNA sequence of Figure 8 (SEQ ID NO:3);
- c) the DNA sequence of Figure 9 (SEQ ID NO:5);
- d) the DNA sequence of Figure 10 (SEQ ID NO:7);
- e) analogues or derivatives of the foregoing DNA sequences;
- f) DNA sequences degenerate to any of the foregoing DNA sequences; and
- g) fragments of any of the foregoing DNA sequences; wherein said sequences encode a product that displays the immunological activity of the *Neisseria meningitidis* 22 kDa surface protein.

13. A DNA sequence encoding at least a portion of at least one antigen of the *Neisseria meningitidis* 22 kDa

surface protein, said sequence being selected from the group consisting of:

- a) the DNA sequence of Figure 1 (SEQ ID NO:1);
 - b) analogues or derivatives of the foregoing DNA sequence;
 - c) DNA sequences degenerate to any of the foregoing DNA sequences; and
 - d) fragments of any of the foregoing DNA sequences;
- wherein said sequences encode a product that displays the immunological activity of the *Neisseria meningitidis* 22 kDa surface protein.

14. A DNA sequence according to claim 12, wherein said analog is selected from the DNA of *Neisseria gonorrhoeae*.

15. A DNA sequence according to claim 12, wherein said analog is selected from the DNA of *Neisseria lactamica*.

16. A DNA sequence of the formula of Figure 1 (SEQ ID NO:1) from base 143 to base 667.

17. A DNA sequence of the formula of Figure 1 (SEQ ID NO:1) from base 200 to base 667.

18. A DNA sequence of the formula of Figure 8 (SEQ ID NO:3) from base 116 to base 643.

19. A DNA sequence of the formula of Figure 8 (SEQ ID NO:3) from base 173 to base 643.

20. A DNA sequence of the formula of Figure 9 (SEQ ID NO:5) from base 208 to base 732.

21. A DNA sequence of the formula of Figure 9 (SEQ ID NO:5) from base 265 to base 732.
- 5 22. A DNA sequence of the formula of Figure 10 (SEQ ID NO:7) from base 241 to base 765.
23. A DNA sequence of the formula of Figure 10 (SEQ ID NO:7) from base 298 to base 765.
- 10 24. A fragment of a DNA sequence according to claim 13, wherein said fragment is selected from the group consisting of: one of the peptides illustrated in Figure 15 (SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24,, SEQ ID NO:25, and SEQ ID NO:26).
- 15 25. A fragment of a DNA sequence comprising from amino acid 31 to amino acid 55 of Figure 1 (SEQ ID NO:1).
- 20 26. A fragment of a DNA sequence comprising from amino acid 51 to amino acid 86 of Figure 1 (SEQ ID NO:1).
- 25 27. A fragment of a DNA sequence comprising from amino acid 110 to amino acid 140 of Figure 1 (SEQ ID NO:1).
- 30 28. A recombinant DNA molecule comprising a DNA sequence selected from the group consisting of the DNA sequences of claims 13, 16, or 17, and one or more expression control sequences operatively linked to the DNA sequence.

29. A recombinant DNA molecule comprising a DNA sequence selected from the group consisting of the DNA sequences of claims 14, 15, or any one of claims 18 to 27, and one or more expression control sequences operatively linked to the DNA sequence.
30. The recombinant DNA molecule of claim 28, wherein said expression control sequence is an inducible expression vector.
31. The recombinant DNA molecule of claim 29, wherein said expression control sequence is an inducible expression vector.
32. The recombinant DNA molecule of claim 30 or 31, wherein said vector is induced by stimuli selected from: temperature, presence of lactose, and presence of IPTG.
33. The recombinant DNA molecule of claim 32, wherein said vector is selected from: λ PL, λ PR, TAC, T7, T3, LAC, and TRP promoters.
34. A plasmid selected from the group consisting of: pNP2202, pNP2203, and pNP2204.
35. A unicellular host transformed with a recombinant DNA molecule of claim 28.
36. A unicellular host transformed with a recombinant DNA molecule of claim 29.

37. The unicellular host according to claim 35 or 36,
wherein the host is selected from the group consisting
of: strains of *E.coli* JM109, *E.coli* BL21(DE3), *E.coli*
DH5 α F'IQ, *E.coli* W3110, *E.coli* JM105, *E.coli* BL21,
5 *E.coli* TOPP1, *E.coli* TOPP2, and *E.coli* TOPP3.
38. The unicellular host according to claim 35 or 36,
wherein the host is selected from the group consisting
of strains of *E.coli* JM109 and *E.coli* BL21(DE3).
- 10 39. A *Neisseria meningitidis* 22kDa surface protein in
substantially pure form obtained by the culturing of a
unicellular host according to claim 35 or 36 and
isolating said protein.
- 15 40. A polypeptide coded for by a DNA sequence of any one
of claims 13, 16 and 17.
- 20 41. A polypeptide coded for by a DNA sequence of any one
of claims 14, 15 and 18 to 27.
42. A method for producing a DNA sequence comprising the
steps of culturing the unicellular host of claim 35 or
36 and isolating said DNA sequence.
- 25 43. A method for producing a polypeptide comprising the
steps of culturing the unicellular host of claim 35 or
36 and isolating said polypeptide.
- 30 44. A polypeptide in substantially pure form as obtained
by the method of claim 43.

45. A method for isolating the antigen of claim 1 comprising:
- a) isolating a culture of *Neisseria meningitidis* bacteria,
 - 5 b) isolating an outer membrane portion from the culture of the bacteria; and
 - c) isolating said antigen from the outer membrane portion.
- 10 46. The method of claim 45, wherein step (c) includes the additional steps of treating the outer membrane portion with proteinase K followed by protein fractionation.
- 15 47. A pharmaceutical composition comprising one or more antigens or fragments thereof according to any one of claims 1 to 5, 8, 13, 16, and 17.
- 20 48. A pharmaceutical composition comprising one or more antigens or fragments thereof according to claim 40.
49. A pharmaceutical composition comprising one or more antigens or fragments thereof according to claim 41.
- 25 50. A pharmaceutical composition comprising one or more antigens or fragments thereof according to any one of claims 6, 7, 9, 12, 14, 15, and 18 to 27.
- 30 51. The pharmaceutical composition of claim 49, which is a vaccine.
52. The pharmaceutical composition of claim 50, which is a vaccine.

53. The pharmaceutical composition of claim 49, further comprising one or more pharmaceutically acceptable excipients.
- 5 54. The pharmaceutical composition of claim 50, further comprising one or more pharmaceutically acceptable excipients.
- 10 55. A method for preventing infection of a patient by *Neisseria meningitidis* comprising the administration of a pharmaceutically effective amount of the vaccine of claim 51 or 52.
- 15 56. The use of a pharmaceutically effective amount of the *Neisseria meningitidis* 22kDa surface protein or a fragment, analogue, or derivative thereof for the prevention of *Neisseria meningitidis* infection in humans.
- 20 57. The use of a pharmaceutically effective amount of the *Neisseria meningitidis* 22kDa surface protein or a fragment, analogue, or derivative thereof for the prevention of *Neisseria gonorrhoeae* infection in humans.
- 25 58. The use of the *Neisseria meningitidis* 22 kDa surface protein or a fragment, analogue, or derivative thereof for the manufacture of a vaccine for the prevention of *Neisseria meningitidis* infection in humans.
- 30 59. The use of the *Neisseria meningitidis* 22 kDa surface protein or a fragment, analogue, or derivative thereof for the manufacture of a vaccine for the prevention of *Neisseria gonorrhoeae* infection in humans.

60. An antibody or fragment thereof that specifically binds to a protein with a molecular weight of approximately 22 kilodaltons present on greater than 50% of known strains of *Neisseria meningitidis*.
61. The antibody or fragment of claim 60 that specifically binds to about 99% of known strains of *Neisseria meningitidis*.
62. The antibody or fragment of claim 60 which is a monoclonal antibody or fragment thereof.
63. The monoclonal antibody or fragment of claim 62 which is of murine origin.
64. The monoclonal antibody or fragment of claim 63 which is of an IgG isotype.
65. The monoclonal antibody or fragment of claim 62 which is Me-1, Me-2, Me-3, Me-5, Me-6, or Me-7.
66. The monoclonal antibody of claim 62 which is the monoclonal antibody Me-1 or Me-7.
67. A method for isolating the antibody of claim 60 comprising:
- a) introducing a preparation of *Neisseria meningitidis* into a mammal; and
 - b) isolating serum from the mammal containing said antibody.
68. A method for isolating the monoclonal antibody of claim 62 comprising:

- a) introducing a preparation of *Neisseria meningitidis* to antibody producing cells of a mammal;
b) fusing the antibody producing cells with myeloma cells to form hybridoma cells; and
5 c) isolating said monoclonal antibody from the hybridoma cells.

69. A pharmaceutical composition comprising one or more antibodies or fragments thereof according to any one
10 of claims 60-66.

70. The pharmaceutical composition of claim 69 which is a vaccine.

15 71. The pharmaceutical composition of claim 69, further comprising a pharmaceutically acceptable excipient.

(72.) The pharmaceutical composition of claim 69, wherein the antibody is Me-1 or Me-7.

20 73. A method for treating a patient infected with or suspected of being infected with *Neisseria meningitidis* comprising the administration of a pharmaceutically effective amount of the vaccine of
25 claim 70.

74. A method for the detection of *Neisseria meningitidis* antigen in a biological sample containing or suspected of containing *Neisseria meningitidis* antigen
30 comprising:

- a) isolating the biological sample from a patient;
b) incubating the antibody or fragment of claim 60 with the biological sample to form a mixture; and

c) detecting specifically bound antibody or bound fragment in the mixture which indicates the presence of *Neisseria meningitidis* antigen.

5 75. The method of claim 72 wherein the antibody is Me-1 or Me-7.

76. A method for the detection of antibody specific to *Neisseria meningitidis* antigen in a biological sample
10 containing or suspected of containing said antibody comprising:

- a) isolating the biological sample from a patient;
b) incubating the antigen or fragment of claim 1 with the biological sample to form a mixture; and
15 c) detecting specifically bound antigen or bound fragment in the mixture which indicates the presence of antibody specific to *Neisseria meningitidis* antigen.

20 77. The method of claim 76 wherein the antigen is the *Neisseria meningitidis* 22 kDa surface protein.

78. A method for the detection of pathogenic *Neisseria* bacteria in a biological sample containing or
25 suspected of containing such bacteria comprising:
a) isolating the biological sample from a patient;
b) incubating a DNA probe having the DNA sequence of claim 13 with the biological sample to form a mixture; and
30 c) detecting specifically bound DNA probe in the mixture which indicates the presence of *Neisseria* bacteria.

79. A method for the detection of pathogenic *Neisseria* bacteria in a biological sample containing or suspected of containing such bacteria comprising:
- a) isolating the biological sample from a patient;
 - b) incubating a DNA probe having the DNA sequence of claim 12 with the biological sample to form a mixture; and
 - c) detecting specifically bound DNA probe in the mixture which indicates the presence of *Neisseria* bacteria.
80. The method of claim 78 wherein the DNA probe has the 525 base pair sequence of Figure 1 (SEQ ID NO:1).
81. The method of claim 78 wherein the DNA probe has a portion of the 525 base pair sequence of Figure 1 (SEQ ID NO:1).
82. The method of claim 79 wherein the DNA probe has the full or a portion of the 528 base pair sequence of Figure 8 (SEQ ID NO:3).
83. The method of claim 79 wherein the DNA probe has the full or a portion of the 525 base pair sequence of Figure 9 (SEQ ID NO:5).
84. The method of claim 79 wherein the DNA probe has the a portion or the full 525 base pair sequence of Figure 10 (SEQ ID NO:7).
85. The method of claim 78 wherein the DNA probe is an oligomer having a sequence complementary to at least about 6 contiguous nucleotides of the *Neisseria*

meningitidis 22 kDa surface protein of Figure 1 (SEQ ID NO:1).

86. The method of claim 79 wherein the DNA probe is an oligomer having a sequence complementary to at least about 6 contiguous nucleotides of the *Neisseria meningitidis* 22 kDa surface protein of sequences selected from: Figure 8 (SEQ ID NO:3), Figure 9 (SEQ ID NO:5), and Figure 10 (SEQ ID NO:7).

87. The method of claim 85 or 86 which further comprises:

- a) providing a set of oligomers which are primers for a polymerase chain reaction method and which flank the target region; and
- b) amplifying the target region via the polymerase chain reaction method.

88. A method for the detection of *Neisseria meningitidis* in a patient comprising:

- a) labeling the antibody or fragment of claim 60 with a detectable label;
- b) administering the labeled antibody or labeled fragment to the patient; and
- c) detecting specifically bound labeled antibody or labeled fragment in the patient which indicates the presence of *Neisseria meningitidis*.

89. The use of a pharmaceutically effective amount of an antibody specific to the *Neisseria meningitidis* 22 kDa surface protein for the prevention of *Neisseria meningitidis* infection in humans.

90. The use of the *Neisseria meningitidis* 22 kDa surface protein or a fragment, analogue, or derivative thereof

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